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## Review Article

### PHYTO-MEDICINAL EFFECTS OF *SYZYGIUM CUMINI* ON DIABETES: A REVIEW

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**Keywords:** *Syzygium cumini*, Phytochemicals, Hypoglycemic Effects, Biochemical Effects.

#### ABSTRACT

*Diabetes* is a major public health problem which has been increasing day by day throughout the world with an alarming rate. In recent years, several plant extracts have been examined for their anti-diabetic properties to identify alternative treatment strategies that pose less risk for diabetes. It has been shown that different parts of these plants are collected from diverse regions and administered in different pharmaceutical preparations. The aim of the present review is to provide an overview of the phytochemicals present in *S. cumini* plants and their potent anti-diabetic activity, toxicological and biological effects of these plant extracts, their current state, limitation and future prospects in developing countries that are not included in the European Pharmacopoeia. In addition, a prospective research result of synergistic use of this plant with other plant (*Ficus racemosa*) done presently in our laboratory has been included. Based on the available evidence, we highlight the ways in which their therapeutic potential can be properly harnessed and provide scientific evidence for the discovery of novel leads for herbal drug development.

#### INTRODUCTION

Diabetes mellitus (DM) is a most common form of diabetes remains a major health care problem worldwide both in developing and developed countries.<sup>[1]</sup> It is a metabolic disorder complex in nature, resulting in either insulin insufficiency or insulin dysfunction with disturbance of carbohydrate, fat, and protein metabolism and classically characterized by hyperglycemia with other clinical presentations such as polyuria, polydipsia, polyphagia, fatigue and irritability.<sup>[2]</sup> Worldwide in the years 2012 to 2014, diabetes is estimated to have resulted in 1.5 to 4.9 million deaths per year and diabetes prevalence in 2019 is estimated to be 9.3% (463 million people) making it the 8<sup>th</sup> leading cause of death.<sup>[3,4]</sup>

Hyperglycemia can be reversed by a variety of measures. Administration of exogenous insulin is the treatment for all type-1 diabetic patients and for some type-2 patients who do not achieve adequate blood glucose control with oral hypoglycemic drugs. Insulin therapy has several drawbacks like insulin resistance, anorexia, brain atrophy and fatty liver in chronic treatment.<sup>[5,6]</sup> Current drugs used in

diabetes management can be categorized into three groups. Drugs in the first group (sulphonylureas such as glibenclamide, the glinides, insulin analogs etc.) increase endogenous insulin availability. The second group of drugs (thiazolidinediones) enhances the sensitivity of insulin. The third group comprises the  $\alpha$ -glucosidase inhibitors such as acarbose, which reduce the digestion of polysaccharides and their bioavailability.<sup>[7, 8]</sup> All the existing therapies however have limited efficacy, limited tolerability and/or significant mechanism based side effects.<sup>[9,10]</sup> Increasing side effects of conventional anti-diabetic medicine are alarming the world, so there is an important and immense need of doing extensive research work towards the anti-diabetic herbal drugs.<sup>[11]</sup>

Phyto-medicine is used to treat human illness since ancient times, due to their less and non-toxic nature.<sup>[12]</sup> A variety of ingredients present in medicinal plants are thought to act on a variety of targets by various modes and mechanisms. They have potential to impart therapeutic effect in complicated disorders like diabetes and its

complications.<sup>[13]</sup> *Syzygium cumini* is one of them and is being claimed in having good effect for decreasing the plasma blood sugar level in diabetic patients and also can be utilized in conditions/ complications related to diabetes and as a supportive in diabetes.<sup>[14]</sup> It has been reported to be used in numerous complementary and alternative medicine systems of India and before the discovery of insulin, was a frontline anti-diabetic medication even in Europe.<sup>[15]</sup>

The present review is aimed at providing in-depth information about the anti-diabetic potential and bioactive compounds present in *Syzygium cumini*, based on article published in various scientific journals for ensuring the safety, standardization, efficacy, quality, availability and preservation of this herbal drug by policy-makers, health professionals as well as the general public.

#### DATA INCORPORATION

The present review covers the literature available from 1956 to 2019. The searched articles were screened initially by title and abstract in context to the interest of the study. The ethno-botanical information was collected from various journals, books, theses and electronic search (Google Scholar, Pub med, Science Direct, Springer link etc.) for publications on *S. cumini* plants, used in diabetes management regarding their effectiveness, pharmacological effects, and safety. 'Diabetes' and 'Plant name – accepted or synonyms' were used as key words for the primary searches. Information was also added from the local study (The Bangladesh population based diabetes and eye study), local agencies (Diabetic Association of Bangladesh), Local journals and the research work on *S. cumini* in the universities of Bangladesh. Moreover, many published Bangla (Mother tongue of Bangladesh and some parts of India) articles about these two plants are translated in English and included in this review, to make this knowledge available to the international community.

#### PLANT DESCRIPTION

*Syzygium cumini* (Family: Myrtaceae) is a polyembryonic species, a tropical fruit tree of great economic importance.<sup>[16]</sup> It is a large evergreen tree up to 30 meters height and girth of about 3.6 meters with a bole up to 15 meters, with smooth, glossy turpentine-smelling leaves. The bark is scaly gray and the trunk is forked. There are fragrant white flowers in branched clusters at stem tips and purplish-black oval edible berries. The berries contain only one seed. The taste is generally acidic to fairly sweet but astringent. This tree is known to have grown in Indian subcontinent and in other regions of South Asia such as Nepal, Burma, Sri

Lanka, Indonesia, Pakistan and Bangladesh from ancient time.<sup>[15]</sup>

#### Scientific classification

Kingdom: Plantae

Order: Myrtales

Family: Myrtaceae

Genus: *Syzygium*

Species: *Syzygium cumini*

**Synonyms:** *Eugenia jambolana* Lam., *Myrtus cumini* Linn., *Syzygium jambolana* DC.,

*Syzygium jambolanum* DC., *Eugenia djouant* Perr., *Calyptanthus Jambolana* Willd., *Eugenia cumini* (Linn.) Druce. and *Eugenia Caryo phyllifolia* Lam.

Common names: Jambolan, Jambul, Black plum, Java plum, Portuguese plum, Malabar plum,

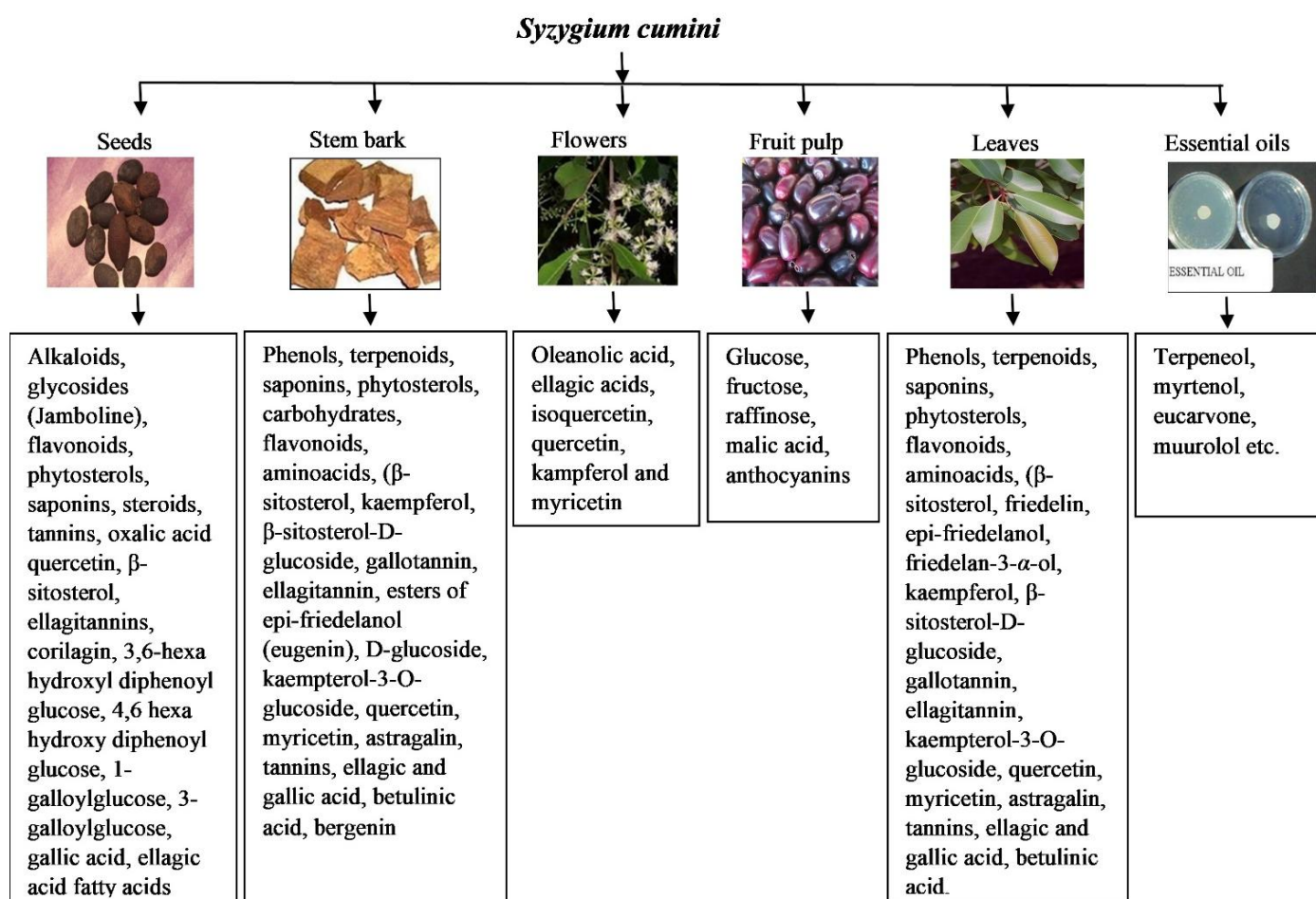
Purple plum, Jamaica and damson plum, Indian blackberry, Jamblang, Jamun etc.

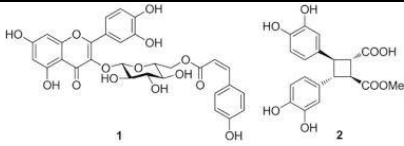
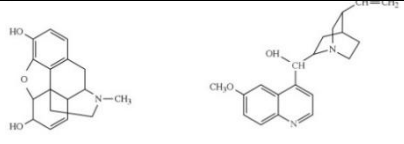
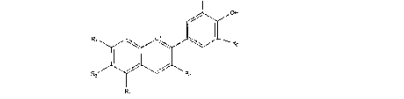
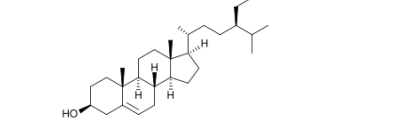
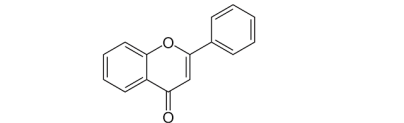
#### CHEMICAL CONSTITUENTS

All parts of the *Syzygium cumini* plants such as Bark,<sup>[17]</sup> Seed,<sup>[18,17,19]</sup> Leaves,<sup>[20,18,19]</sup> Fruit,<sup>[19]</sup> Root,<sup>[18]</sup> Flowers <sup>[20, 18]</sup> possess diverse phytochemicals. The active ingredient in Jaman seed is mycaminose. The mechanism of action of mycaminose is similar to glibenclamide (a standard drug used for many years as anti-diabetic).<sup>[21]</sup> The other chemical constituents responsible for the inhibition of glucose are terpenoids, glycosides, saponins, flavanoids, phenols etc. Jamun contains an important glycoside namely Jambolin which prevents the conversion of starch into sugar thereby helps in controlling the blood sugar.<sup>[11]</sup>

Although almost all parts of the *S. cumini* has anti-diabetic activity, seed kernel was used in many research experiments. Kumar in their study administered Mycaminose at the dose of 50 mg / kg, ethyl acetate and methanol extracted compounds of *Syzygium cumini* seeds at the dose of 200 mg/kg and 400 mg/kg respectively which was administered to streptozotocin-induced diabetic rats and found that Mycaminose and ethyl acetate and methanol extracts of *Syzygium cumini* Linn. produced significant reduction in blood glucose level.<sup>[22]</sup> Achrekar S concluded in their study that the extract of jaman pulp from fruit of *Eugenia jambolana* showed hypoglycemic activity. This report is the first evidence of such activity in relation to pulp. The effect of pulp was seen in 30 min, while the seeds of the same fruit required 24 hour.<sup>[23]</sup>

The chemical constituents of different parts are enlisted in Fig.1 and phytochemicals which have potent anti-diabetic principle are given in Table 1.

Figure 1: Phytochemical constituents present in the *Syzygium cumini* plantTable 1: Phytochemicals and their anti-diabetic principles of *Syzygium cumini*

Sl No.	Phyto chemicals	Chemical structure	Anti-diabetic principles with references
1	Acylated flavonol glycosides		Have potential hypoglycemic effect. <sup>[21]</sup>
2	Alkaloids		Well known for their anti-diabetic activities by different mechanisms, Jambosine slows down the diastatic conversion of starch into sugar. <sup>[24]</sup>
3	Anthocyanins		Stimulate insulin secretion from rodent pancreatic $\beta$ -cells in vitro. <sup>[25-26]</sup>
4	$\beta$ -sitosterol		Have potential anti-diabetic activities. <sup>[27]</sup>
5	Flavonoids		Regenerate damaged pancreatic $\beta$ -cells in diabetic animals; Inhibitory effect on c'AMP-phosphor-reduces blood glucose concentration; Have anti-oxidant and free radical scavenging properties responsible for the anti-diabetic activity. <sup>[27-30]</sup>

6	Glucoside (Jamboline and ellagic acid)		Ability to check the conversion of starch into sugar in case of excess production of glucose; Glycosidases remove sugar residues; Jamboline slows down the diastatic conversion of starch into sugar.[22, 24, 31-32]
7	Myricetin		Lower blood glucose through improved glucose utilization in diabetic animals; Has potential hypoglycemic effect.[21, 26, 33-34]
8	Polyphenolic compounds		Have anti-oxidant and free radical scavenging properties that might be responsible for the anti-diabetic activity.[28]
9	Quercetin		Promote regeneration of the pancreatic islets and increase insulin release; Has potential hypoglycemic effect.[21, 26, 35]
10	Saponins		Well known for their anti-diabetic activities by different mechanisms.[36]
11	Tannins		Well known for their anti-diabetic activities by different mechanisms; Known to possess anti-diabetic activity; Have potential hypoglycemic effect.[21, 36]

### SUMMARY OF EXPERIMENTAL PROCEDURES

Scientists used a number of experimental methods to show the anti-diabetic potentials of *Syzygium cumini*. These methods are summarized in Table 2.

**Table 2: Experimental methods followed by various scientists for *Syzygium cumini***

Plant parts	Animal model used (In vivo)	Extract type	Dose (mg/kgbw)	Duration	Route	Control
Seeds	Male Wistar albino rat	Ethanollic	250, 500 & 750	15, 30 and 45 days	Oral	Negative control.[37]
Seeds	Albino rat of either sex	Methanolic	500	Single dose	Oral	Positive control.[25]
Seeds	Albino rat of either sex	Methanolic	300	7 days	Intra peritoneal	Positive & negative control.[38]
Seeds	Female albino Wistar rat	Gum Acacia suspension	250, 500 or 1000	15 days	Oral	Positive & negative control.[39]
Seed kernel	Male Sprague Dawley rat	Ethanollic	200	Single dose	Oral	Positive & negative control.[40]
Seed kernel	Male albino rat	Aqueous suspension	4000	Single dose	Oral	Positive & negative control.[41]
Seeds	Long-Evans female rat	Ethanollic extract & Seed powder	1250	21 days	Oral	Positive & negative control.[42]
Seeds	Long Evan's rat	Methanolic	100 & 300	21 days	Oral	Positive & negative control.[43]



Bark	Male Wistar albino rat	Aqueous	300	45 days	Oral	Positive & negative control. <sup>[44]</sup>
Pulp	Female Wistar rat	Aqueous	100 & 200	15 days	Oral	Positive & negative control. <sup>[45]</sup>
Fruit-pulp	Albino rabbit	Partially purified water extract	25	Single dose	Oral	Negative control. <sup>[46]</sup>
Leaves	Male Wistar albino rat	Aqueous	100 & 200	6 weeks	Oral	Negative control. <sup>[36]</sup>
Seeds	Wister albino rat of either sex	Aqueous	400	4 weeks	Oral	Negative control. <sup>[47]</sup>
Seeds	Wistar albino rat of either sex	Petroleum ether, acetone, methanol and water extracts	100	21 days	Oral	Positive & negative control. <sup>[48]</sup>
Seeds	Wister albino male rat	Aqueous	250 & 500	4 months	Oral	Positive & negative control. <sup>[49]</sup>
Seeds	Swiss albino mice	Aqueous	150 & 250	21 days	Oral	Negative control. <sup>[50]</sup>

N.B: mg: Milligram; gbw: Gram Body Weight; kgbw: Kilogram Body Weight

## Effects of Extracts

### 1. Physiological effects (Body weight)

The effect of different parts of *Syzygium cumini* on body weight of preclinical models (mostly rodents) have been investigated by several investigations. These preclinical studies are with mixed results as a few studies have shown that *S. cumini* decreased the total body weight<sup>[42,43]</sup> whereas the majority of the preclinical reports have indicated that Jamun increased the body weight in rodent models of diabetes and clinical setting.

The ethanol extract of seeds has been shown to increase (24.18%) body weight in alloxan monohydrate induced diabetic rats.<sup>[37]</sup> The administration of methanol extract of seed at 300mg/kgbw in diabetic rats has also been reported significantly increased body weight in diabetic rats.<sup>[38]</sup> Likewise, other studies on aqueous seed extract has been found to increase body weight in the diabetic rats.<sup>[39, 45]</sup> The administration of aqueous extract of leaves at 100mg/kgbw and 200mg/kgbw in male wister albino rats has also increased the body weight significantly (12.7% and 16% respectively).<sup>[36]</sup>

According to the literature, *S. cumini* seed ethanolic extract @ 500 mg/kgbw showed the best improvement in body weight of experimental animals.<sup>[37]</sup>

### 2. Hypoglycemic effects

Excessive hepatic glycogenolysis and gluconeogenesis associated with decreased utilization of glucose by tissues is the fundamental mechanism underlying hyperglycemia in the diabetic state.<sup>[51]</sup> Researchers used a number of doses in order to scientifically validate the therapeutic preparation of

*Syzygium cumini* plants in the control of hyperglycemia (Table 3). Majority of the preclinical reports have indicated that different parts of *S. cumini* reduced blood sugar levels in rodents and human being.

The administration of aqueous seed extract of Jamun at a dose of 1 g/kg b. wt. in diabetic rats has been reported to produce hypoglycaemic effect in the blood.<sup>[52]</sup> The lyophilized powder of aqueous seed extract has also been reported to decrease the blood glucose level in diabetic mice and rats.<sup>[53, 54]</sup> Similarly, Jamun aqueous seed extract consisting of gummy fibres has been highly effective in controlling diabetes in alloxan induced diabetes in rats. However, in contrast, the aqueous extract devoid of gummy fibre did not have any effect on blood sugar level.<sup>[24]</sup>

The administration of ethanol extract of Jamun seeds depleted the blood serum glucose levels in the streptozotocin induced diabetic rats in some other studies.<sup>[25,26]</sup> The aqueous and methanol extracts of root, stem bark, leaf and seed extracts of Jamun has been reported to lower serum glucose levels in alloxan-induced diabetes in male Sprague Dawley rats in an earlier study.<sup>[27]</sup> Supplementation of Jamun seed powder in human diabetic subject for 30 days reduced the fasting and post prandial blood glucose levels.<sup>[28]</sup> In a double blinded control clinical trial, feeding of 10g of Jamun seed powder up to 90 days to diabetic patients reduced the fasting blood glucose levels by 9%, 18%, and 30% and post prandial glucose by 8%, 15%, and 22% after 30, 60, and 90 days, respectively.<sup>[29]</sup>

Recently, the administration of ethanol extract of Jamun seeds and fruits for 60 days reduced serum

glucose level in hyperglycaemic/diabetic rats and the former was more effective than the later.<sup>[30]</sup> Although *Syzygium cumini* (seed aqueous extract) can reduce blood glucose levels in high fructose diet induced diabetic rats, in a dose dependent (200mg/kg, 400mg/kg and 800mg/kg) manner, but in euglycemic animals it had no effect on the blood glucose levels.<sup>[31]</sup>

Some other research investigations about hypoglycemic effects of *S. cumini* has been showed in a tabular form (Table 3). According to the literature, petroleum ether soluble fraction of *S. cumini* seed methanolic extract @ 300 mg/kgbw (76.82%)<sup>[43]</sup> and seed ethanolic extract @ 500 mg/kgbw (69%)<sup>[37]</sup> showed the best hypoglycemic results (Table 3).

**Table 3: Hypoglycemic changes reported by various scientists on application of *Syzygium cumini***

Dose	Extract type	Decrease	Reference
15 days: (25 mg/100gbw), (50 mg/100gbw), (75mg/100gbw); 45 days: (250 mg/kgbw) <b>*(500 mg/kgbw)</b> (75mg/100gbw)	Ethanolic extract of seed	24.00% 46.00% 50.00% 50.00% <b>69.00%</b> 58.00%	[37]
300 mg/kgbw:	Methanolic extract of leaf	26.39%	[38]
250 mg/kgbw: 500 mg/kgbw: 1000 mg/kgbw:	Seed powder suspension in 2% gum acacia	13.00% 30.00% 46.00%	[39]
Single dose: 2h Multiple doses: between 9th and 11th day	Seed kernel extract	14.28% 28.6-34.2%	[40]
4000 mg/kgbw	Seed kernel extract	12.92%	[41]
1250mg/kgbw 1250mg/kgbw	Seed powder Ethanolic extract of seed	29.18% 38.37%	[42]
100 mg/kgbw <b>*300 mg/kgbw</b>	Petroleum ether soluble seed	73.19% <b>76.82%</b>	[43]
100 mg/kgbw 300 mg/kgbw	Carbon tetrachloride soluble seed	11.51% 18.79%	
100 mg/kgbw 300 mg/kgbw	Dichloromethane soluble seed	55.03% 42.82%	
100 mg/kgbw 300 mg/kgbw	Aqueous soluble seed	20.02% 14.22%	
100 mg/kgbw 200 mg/kgbw	Aqueous extract of pulp	46.30% 51.23%	[45]
300 mg/kgbw	Extract of bark	68.56%	[44]
400 mg/kgbw	Aqueous extract of seed	37.34%	[47]
100 mg/kgbw 200 mg/kgbw	Aqueous extract of leaf	54.28% 53.81%	[36]
100 mg/kgbw	Methanol extract of seed	56.00%	[48]

**N.B: mg: Milligram; gbw: Gram Body Weight; kgbw: Kilogram Body Weight, \* Dose for best hypoglycemic results**

### Biochemical effects

#### Liver Glycogen

The decrease of liver glycogen observed in diabetic animal may be due to lack of insulin in diabetic state or oxidative stress by diabetes may inactivate

the glycogen synthetase.<sup>[32]</sup> In the view of glycogen level, there may be three possible way of antidiabetogenic action, one possible way may be

increased insulin level. Other possible ways of anti-diabetic action of *Syzygium cumini* may be by preventing the inactivation of the glycogen synthetase and by synthesize the glycogen synthetase.

The effect of *S. cumini* seed powder (250, 500 or 1000 mg/kg) on diabetic rats showed a difference in liver glycogen ( $50 \pm 6.8$ ,  $52 \pm 7.5$  vs normal control  $90 \pm 6.6$   $\mu\text{g/g}$  of liver tissue,  $P < 0.001$ ).<sup>[39]</sup> But *S. cumini* seed powder and ethanol extract (1.25/kgbw) has no significant effect on liver glycogen in streptozotocin (STZ) induced type 2 diabetic rats after 21 days of consecutive feeding.<sup>[42]</sup> The administration of ethanolic extract of jamun seeds 100 mg/kg of body weight increased liver glycogen significantly on streptozotocin-induced diabetic rats.<sup>[33]</sup>

According to the literature, *S. cumini* leaves aqueous extract (100 mg/kgbw) and ethanolic extract of seed (500 mg/kgbw) brought the increased levels of glycogen (189.40%) to almost normal glycogen in liver respectively (Table 4).

#### Cholesterol, triglyceride, HDL & LDL

It is well known that in uncontrolled diabetes mellitus, there will be an increase in total cholesterol, triglycerides and LDL cholesterol associated with decrease in HDL cholesterol.<sup>[34]</sup> *Syzygium cumini* extracts may inhibit the pathway of cholesterol synthesis and increased HDL/LDL ratio due to the activation of LDL receptors in hepatocytes, which is responsible for taken up LDL into the liver and reduce the serum LDL level.

The seed extract of Jamun showed an alleviation in the total serum cholesterol (TC)/high density lipoprotein cholesterol (HDL-c) ratio and the amount of serum low density lipoprotein cholesterol (LDL-c) in alloxan-induced diabetic rabbits.<sup>[35]</sup> Administration of the ethanolic extract of different parts of jamun seeds such as whole seed, kernel, and seed coat 100 mg/kg of body weight decreases significantly the levels of cholesterol on streptozotocin-induced diabetic rats.<sup>[33]</sup> But chronic feeding of *S. cumini* powder and ethanol extract did not significantly change the total cholesterol and triglyceride levels in type 2 diabetic rats. The beneficial HDL cholesterol level increased and a lowering of LDL cholesterol level was observed.<sup>[42]</sup> Likewise, numerous other studies on different parts of *S. cumini* (aqueous extract of leaf, ethanolic extract of seed and fruits) has also been found to increase the HDL and decrease the LDL cholesterol level.<sup>[45,30,36,55]</sup> The active principles isolated by passing ethanol seed extract fraction of Jamun on sephadex gel did decrease triglycerides and total cholesterol and raised the HDL cholesterol level in the alloxan-induced diabetic rats.<sup>[56]</sup>

According to the literature, *S. cumini* ethanolic extract of leaf (125mg/kgbw) and (500 mg/kgbw) significantly decrease serum cholesterol (64.17%) and triglycerides (68.42%) levels respectively.<sup>[57]</sup> HDL levels were increased (165.08%) after treatment with *S. cumini* leaf aqueous extract (200mg/kgbw). The elevated levels of serum LDL cholesterol were significantly (61.9%) decreased after treatment with aqueous extract of *S. cumini* pulp (200mg/kgbw) (Table 4).

**Table 4: Biochemical changes (Glycogen, Cholesterol, Triglyceride, HDL & LDL) on administration of *S. Cumini***

Dose (mg/kgbw)	Glycogen	Cholesterol		Triglyceride		HDL	LDL	Ref
	Normal or Increased state	Increase (%)	Decrease (%)	Increase (%)	Decrease (%)	Increase (%)	Decrease (%)	
30 days: 250 & 500	Increased intensity of glycogen Almost no glycogen	- -	- -	- -	- -	- -	- -	[37]
750	Almost normal glycogen	-	-	-	-	-	-	
45 days: 250 & 500*	Almost no glycogen	-	-	-	-	-	-	
750	Almost no glycogen localization	-	-	-	-	-	-	
500 1000	66.67%, 73.33%	- -	- -	- -	- -	- -	- -	[39]

100*	189.40%	-	46.23	-	41.07	83.73	47.83	[36]
200****	169.70%	-	48.15	-	42.82	165.08	59.65	
100	-	-	19.17	-	28.17	23.86	34.15	[45]
200*****	-	-	29.59	-	46.37	44.11	61.89	
125**	-	-	1h: 64.18 2h: 39.46 3h: 59.14	-	1h: 13.15 2h: 53.04 3h: 61.88	-	-	[57]
250	-	-	1h: 08.29 2h: 08.11 3h: 35.91	1h: 47.20 2h: 110.0 3h: 16.74	-	-	-	
500***	-	1h: 06.95 3h: 03.07	2h: 05.99	-	1h: 57.99 2h: 59.51 3h: 68.43	-	-	

N.B: mg: Milligram; gbw: Gram Body Weight; kgbw: Kilogram Body Weight; h: Hour; HDL: High Density Lipoprotein; LDL: Low Density Lipoprotein; Best dose for \*glycogen, \*\*Cholesterol, \*\*\*Triglyceride, \*\*\*\*HDL and \*\*\*\*\*LDL respectively

### Histological effects (Pancreas and Liver)

In diabetic animals degenerative changes were seen as well as regular arrangement of  $\alpha$  and  $\beta$  cells were disturbed. But after the treatment of *Syzygium cumini* extract, when blood sugar came down to normal level, histology of pancreas and liver have showed improvement.

Aqueous extract of *S. cumini* bark at a dose of 1g/kg of body weight showed the positive staining for insulin on cells of the pancreatic duct and connective tissue in the pancreas of diabetic rats which indicates that the bark of *S. cumini* stimulates development of insulin positive cells from the pancreatic duct epithelial cells.<sup>[58]</sup> After 15 days of administration of ethanolic extract of *S. cumini* seed @ 250 mg/kgbw in alloxan-induced diabetic male Wistar albino rat, the islets of langerhans did not show improvement and were small in size or disfigured but after 30 days,  $\beta$  cells achieved granulation although some necrosed areas were still present within islets.<sup>[37]</sup>

According to the literature, *S. cumini* seed ethanolic extract @ 500 mg/kgbw and 750 mg/kgbw showed the best improvement in the histology of pancreas of experimental animals.<sup>[37]</sup>

Ethanolic extract of jamun seed in diabetic rats can recover the damaged liver in a dose dependent manner. Both the dose (250 mg/kgbw and 500mg/kgbw) can recover the hydropic degeneration of liver in a time dependent manner whereas the dose @ 750 mg/kgbw did not show any recovery.<sup>[37]</sup> Supplementation of methanolic extract of *S. cumini* seed @ 300 mg/kgbw also restored the histopathological changes of liver in alloxan induced diabetic rats.<sup>[38]</sup>

According to the literature, *S. cumini* seed ethanolic extract @ 500 mg/kgbw showed the best improvement in the histology of liver of experimental animals.<sup>[37]</sup>

### Current State, Limitations and Future Prospects

The diabetes has been increasing throughout the globe with an alarming rate due to lifestyle changes and it has become a global burden requiring attention of the most populated countries, where its incidence is ever increasing.<sup>[59]</sup> The global diabetes prevalence in 2019 is estimated to be 9.3% (463 million people), rising to 10.2% (578 million) by 2030 and 10.9% (700 million) by 2045.<sup>[4]</sup>

People have become more interested in herbal medicine because the global burden of treatment cost by conventional anti-diabetic medicine is very high and the increasing side effects of these medicines are alarming in the world.

A recent study was conducted on induced diabetic swiss albino mice at the laboratory of Dept. of Anatomy and Histology, Faculty of Veterinary Science, Bangladesh Agricultural University, Bangladesh. The combined ethanolic extract of *S. cumini* @ 250mg/kgbw and *F. racemosa* @ 125mg/kgbw was administered orally once daily for 30 days in comparison to their individual treatments (ethanolic extract of *S. cumini* @ 500mg/kgbw; ethanolic extract of *F. racemosa* @ 250mg/kgbw). The fasting blood sugar was measured in controlled and treated mice at 14 days interval (at 0, 15 & 30 d). Results revealed that the lower dose combination of ethanolic extracts of *S. cumini* and *F. racemosa* were effective ( $p < 0.01$ ). Moreover, the *S. cumini* seed extract had shown a better anti-hyperglycemic activity (36.89%) than that of the *F.*



*racemosa* fruit extract (31.37%) whereas a lower dose combination of these two plant extracts showed the best degree of efficacy (47.09% more effective).<sup>[60]</sup>

From this review study it is clearly demonstrated the efficacy of *Syzygium cumini* in both animal and human models of diabetes. Although *S. cumini* reduce the blood glucose level, however, it's mechanism of action yet to provide. Some reported activities of Jamun suggested that it acts by inhibiting the alpha amylase and alpha glucosidase enzyme activity because of having higher content of tannins. But for exploring the molecular mechanism of action of jamun in various study systems, it is an important and immense need of doing extensive research work towards the anti-diabetic herbal drugs so that can help the present world in a descent and nice way of treating these diseases.

## CONCLUSION

This review provides useful resources to enable a thorough assessment of the profile of *Syzygium cumini* plants and give importance on its use in diabetes management. In every section of the manuscript, a recommendation has also been drawn that would be eventually helpful for the researchers in this realm. The review is also aiming to draw attention of the relevant researchers to expand the use of this plant in ethno-pharmacotherapy and the development of new herbal drugs; as the technology is now extremely powerful than before.

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